

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY  
DEPARTMENT OF PESTICIDE REGULATION  
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

GLYPHOSATE, ISOPROPYLAMINE SALT

SB 950-241, Tolerance # 364, Chemical Code # 1855

December 2, 1986

Revised 12/14/87, 11/18/88, and 11/03/92

I. DATA GAP STATUS

Chronic, rat:	No data gap, no adverse effect
Chronic, dog:	No data gap, no adverse effect
Oncogenicity, rat:	No data gap, possible adverse effect
Oncogenicity, mouse:	No data gap, possible adverse effect
Reproduction, rat:	No data gap, no adverse effect
Teratology, rat:	No data gap, no adverse effect
Teratology, rabbit:	No data gap, no adverse effect

Gene mutation:                      No data gap, no adverse effect

Chromosome:                        No data gap, no adverse effect

DNA damage:                        No data gap, no adverse effect

Neurotoxicity:                      Not required at this time

-----**Note, Toxicology**  
**one-liners are attached**

In the 1-liners below:

  \*\* indicates acceptable study

**Bold face** indicates possible adverse effect

  ## indicates study on file, but not yet reviewed.

File name T921103.

Revised by C. Aldous, 11/03/92

All record numbers through 095055 (Document No. 364-206) have been examined. All records indexed as of 7/08/92 are included (Aldous, 11/03/92).

Note: these pages contain summaries only. Individual worksheets may identify additional effects.

## II. SUMMARY OF TOXICOLOGY INFORMATION

NOTE--NO EPA ONE-LINERS AVAILABLE

## COMBINED -- RAT (Chronic/Oncogenicity)

**\*\*364-207 091579** "Chronic study of glyphosate administered in feed to albino rats", (L.D. Stout and F.A. Ruecker, Monsanto Agricultural Co., Environmental Health Laboratory, St. Louis, MO. Laboratory Project No. MSL-10495, 9/26/90). Glyphosate (Lot XLH-264); 96.5% pure, was administered at concentrations of 0, 2,000, 8,000, or 20,000 ppm in diets of 50 Sprague Dawley rats/sex/group for 24 months. An additional 10 rats/sex/group were designated for 1-year interim sacrifice. NOEL = 8,000 ppm (b.w. decrement in females, basophilic degeneration of the posterior subcapsular lens fibers in males, and increased liver weights in males). In addition, a modest incidence of relatively uncommon tumor type (adrenal cortical carcinomas) was found only in 20000 ppm females (3/50, vs none in other groups of either sex), and is considered a **"possible adverse effect"**. [No NOEL is presumed for neoplasia, since no threshold has been established]. The lack of notable findings up to and including 8000 ppm and the marginal evidence of tumor effects suggest minimal health concerns. **Acceptable.** Additional Record #'s 117131-117133 in Document No. 51834-002 were considered in this review. Kishiyama and Aldous, 11/03/92.

51834-002 117131 Monsanto in-house (EHL) historical control data in support of Record No. 091579, above.

51834-002 117132 Bio/dynamics, Inc. historical control data in support of Record No. 091579, above.

51834-002 117133 Charles River Laboratories historical control data in support of Record No. 091579, above.

## CHRONIC TOXICITY, RAT

002 937658 "Two-Year Chronic Oral Toxicity Study With CP67573 In Albino Rats," IBT 1/14/74, IBT Study No. B564; J. Christopher 7/8/85, Dose levels of 0, 30, 100 or 300 ppm: Invalid

022/043 025282 IBT Summary, Duplicate information of 002 937658.

## CHRONIC TOXICITY, DOG

\*\* 131 037076 "Twelve Month Study of Glyphosate Administered by Gelatin Capsule to Beagle Dogs" (831); Project No. ML-83-137; Monsanto, St. Louis, MO, 11/1/85. Glyphosate technical (96%) given by capsule at 0, 20, 100 or 500 mg/kg/day; 6/sex/group; **No adverse effect** identified; NOEL greater than 500 mg/kg. **Acceptable**. J. Schreider, 7/24/86.

002 937659 "Two-Year Chronic Oral Toxicity Study With CP 67573 in Beagle Dogs". IBT No. 651-00565 (same as J-565, ruled "valid but unacceptable" by EPA); IBT, Northbrook, Illinois, 11/30/73; CP 67573 (Glyphosate) at 0, 30, 100 & 300 ppm in 4 dogs/sex/group; **Insufficient information for adverse effect assessment; Unacceptable** (No pathology summary report; no means or standard deviations presented for summary data; no statistical analysis). J. Christopher, 7/8/85.

022/043 025281 IBT Summary, Duplicate information of 002 937659.

## ONCOGENICITY, RAT

086/122 937682 "A Lifetime Feeding Study of Glyphosate (ROUNDUP Technical) in Rats"; Project No. 77-2062; Bio/dynamics Inc., East Millstone, N.J., 9/18/81. Glyphosate (98.7%) at 0, 3.05, 10.3 & 31.5 mg/kg (30, 100 & 300 ppm) to 50 Sprague-Dawley rats/sex/group for 24 months. **No adverse effects indicated** (J. Christopher had requested additional information on possible

increase in interstitial cell (ISC) tumors in high dose males, but did not consider data to indicate an adverse effect. Historical data in 162 048774 indicate that ISC tumors were incidental). Report complete, but **unacceptable and not upgradeable** (inadequate doses, no toxicity seen at any dose). J. Christopher 7/15/85 & 12/3/85. Subsequent review and rebuttal response (to 162 048774) by C. Aldous, 11/12/86.

NOTE: U.S. EPA required a more rigorous study to supercede this one, which has now been reviewed as Document No. 364-207 (p. 2 of this Summary).

087/123 937681 9/18/81, Pathology Report (Pathology Summary, Summary Incidence Tables, Neoplasm Summary Incidence Tables, Histopathology Incidence Tables, Males (Vol. 2 of 5); Part of 086 937682.

088/124 937680 7/17/81, Histopathology Incidence Tables, Females (vol. 3 of 5); Part of 086 937682. Note: Volume 124 is missing pages 3-117 to 3-183.

125 035836 9/18/81 J. Christopher 12/3/85; Individual Body Weights, Food Consumption & Test Substance Intake Values - Males (Vol. 4 of 5); Part of 086 937682.

126 035837 9/18/81 J. Christopher 12/3/85; Individual Body Weights, Food Consumption & Test Substance Intake Values - Females (Vol. 5 of 5); Part of 086 937682.

127/089 035838 11/9/82 & 11/18/82 J. Christopher 12/3/85; Letters from 2 pathologists regarding increased incidence of thyroid tumors; Supplemental information to 086 937682.

058 937657 9/18/81, Study Summary (11 pages) and 19 pages of text; Partial duplicate of 086 937682.

ONCOGENICITY - MOUSE

**\*\* 076 937660** "A Chronic Feeding Study of Glyphosate (ROUNDUP Technical) in Mice" (832); Project No. 77-2061; Bio/dynamics Inc., Monsanto, St. Louis, Missouri, 7/21/83. Glyphosate technical (99.7%); Dosages of 0, 1000, 5000 & 30000 ppm in diets of CD-1 mice. **Possible oncogenic effect** [equivocal effect on renal tubular epithelial adenomas plus carcinomas (relatively uncommon tumors) in males: incidence of adenomas plus carcinomas = 1, 0, 1 and 3 in 0, 1000, 5000 & 30000 ppm groups, respectively]. General systemic toxicity NOEL = 5000 ppm (effects at 30000 ppm included central lobular hepatocyte hypertrophy in males, central lobular hepatocyte necrosis in males, chronic interstitial nephritis in males, and proximal tubule epithelial basophilia and hypertrophy in females). CDFA/DPR reviews and history of disposition of study: J. Christopher, 7/19/85 (unacceptable, possible adverse effect indicated); J. Remsen Gee, 5/1/86 (unacceptable, possible adverse effect indicated); C. Aldous 11/17/86 and 12/14/87 (Report **acceptable with possible adverse effect** - both reviews). **NOTE: EPA had been requiring a repeat mouse oncogenicity study, but this requirement appears to have been waived on or before the time of the Federal Register document of 3/12/92** (found in Appendix 3, at the end of Document No. 51834-002). See EPA publication, "Guidance for the reregistration of pesticide products containing glyphosate as the active ingredient" (June, 1986).

142 045712 7/21/83; C. Aldous 11/21/86: Toxicology Report (Individual Body weight, Body weight gain, Food consumption, Feed efficiency & Test Substance Intake Values in Male Mice); Volume 2 of 8; Part of 076 937660.

143 045713 7/21/83; C. Aldous 11/21/86: Toxicology Report (Individual Body weight, Body weight gain, Food consumption, Feed efficiency & Test Substance Intake Values in Female Mice); Volume 3 of 8; Part of 076 937660.

144 045714 7/21/83; C. Aldous 11/21/86: Toxicology Report (Physical observations by group; Individual Water Consumption & Hematology Values, Total & Differential Leukocytes, Organ Weights & ratios; Volume 4 of 8; Part of 076 937660.

145 045715 7/21/83; C. Aldous 11/21/86: Pathology Report (Individual Data in male mice killed by design: gross & microscopic findings; Volume 5 of 8; Part of 076 937660.

146 045716 7/21/83; C. Aldous 11/21/86: Pathology Report (Individual data in male mice killed in extremis or found dead (unscheduled deaths)--gross & microscopic findings; Volume 6 of 8; Part of 076 937660.

147 045717 7/21/83; C. Aldous 11/21/86: Pathology Report (Individual data in female mice killed by design: gross & microscopic findings); Volume 7 of 8; Part of 076 937660.

148 045718 7/21/83; C. Aldous 11/21/86: Pathology Report (Individual data in female mice found dead or killed in extremis: gross & microscopic findings; Lesion incidences & Individual fate data for male and female mice; QA Statement; Volume 8 of 8; Part of 076 937660.

128 036060 10/7/85. Examinations of 3 additional sections of each kidney of each male in the primary study 076 937660, by the pathologist who read the original slides. No new renal epithelial tubular tumors were found. [Between the time of the final report and this re-evaluation, a renal epithelial adenoma was found in a control male. This lesion was not observed in the additional sections taken from the same kidney in the present report]. J. Gee, 5/1/86.

163 048775 "Response to SB950 Data Request For Glyphosate, Oncogenicity: Rodent" (8/26/86 Rebuttal). Provided clarifications relating to primary study 076 937660 and historical control data on kidney lesion incidence for CD-1 COBS mice at Bio dynamics. Incidence of tubular adenomas was very low and there were no tubular carcinomas listed, indicating that the finding of 3 such tumors in a group of 50 males was an unusual incidental finding. C. Aldous 11/17/86.

178 063476 "Pathology working group report on glyphosate in CD-1 mice." Report prepared by R. M. Sauer, V.M.D., on 10/10/85. Blind re-reading of all sections of kidneys of all males from primary study 076 937660 by original pathologist and by three other pathologists.

Consensus was that renal tubular cell adenoma and carcinoma incidence was 1, 0, 1 and 3 for groups: control, 1000, 5000 and 30000 ppm respectively. C. Aldous 11/10/87.

178 056111 FIFRA Scientific Advisory Panel: "A set of scientific issues being considered by the agency in connection with the registration standard for Glyphosate." (Meeting date after 1/17/86). Panel noted that renal tumor incidence data is equivocal: age-adjusted tumor incidence data do not demonstrate a statistically significant increase in such tumors based on concurrent controls, nevertheless the incidence at 30000 ppm (the HTD) is quite significant when compared to historical controls. The Panel proposed classification as "Group D" (not classified) and proposed further tests in rats and/or mice to resolve the oncogenicity issue. This evaluation was considered by C. Aldous in 11/10/87 review.

178 056112 "FAO plant and protection paper #77: Report of the joint meeting on pesticide residues." Rome, 9/29/86 - 10/8/86. Report states that glyphosate is of low order toxicity in the major toxicity studies and that "There is no evidence of carcinogenicity."

178 (no record numbers) Additional interpretations associated with the 4/3/87 Rebuttal document by Monsanto Agricultural Co. These were brief memoranda by 4 prominent scientists in tabs "Part 1" through "Part 4": of this volume, who cited statistical and biological evidence for the proposition that glyphosate is not an oncogen. These statements were undoubtedly made available for SAP consideration in 1986, and should be considered by CDFA, should glyphosate come under risk assessment in California.

002 937661 Title: "18-Month Carcinogenic Study With CP67573 in Swiss White Mice," IBT 9/19/73; IBT Study No. B569; J. Christopher 7/8/85; Dose levels of 100 or 300 ppm: Invalid.

022/043 025280 IBT 9/19/73; Summary; Duplicate information of 002 937661.

REPRODUCTION, RAT



057 937677 "A Three Generation Reproduction Study In Rats With Glyphosate," Project No. 77-2063, BDN 77-417; Bio/dynamics Inc., 3/31/81. Glyphosate, lot XHJ-64, 98.7% was administered at 0, 3, 10, and 30 mg/kg/day in diets of CD\* rats; Apparent reproductive effects NOEL > 30 mg/kg/day (No definitive evidence of systemic or reproductive effects at the doses tested). CDFA review dates: J. Christopher, 7/10/85; C. Aldous, 11/19/86 and 12/9/87. Changes in CDFA study status: 7/10/85 review indicated unacceptable study, possible reproductive effect (based on the data then available: volumes 57, 77 and 79): 11/19/86 review indicated unacceptable study, no adverse effects indicated (based on review of previous data plus new data and Monsanto Rebuttal comments of 8/26/86 and 9/30/86 in volumes 164-168). The 12/9/87 review considered the 5/18/87 Monsanto Rebuttal statement, from Doc. #364-179, and did not recommend change of status, which is: **Unacceptable study with no adverse effects indicated**, (no definitive LEL for reproductive effects).

164 048776 Rebuttal (5 pages); Appendix D, Pathology Report,      Terminal Sacrifice  
(Individual gross & microscopic observations, Summary-incidence of microscopic findings); C. Aldous, 11/19/86; Part of 057 937677.

165 048777 Pup selection procedure; Day 21 mean pup weights:      individual and mean  
tables; C. Aldous, 11/19/86; Part of 057 937677.

166 048778 Individual organ and body weights and organ/body and organ/brain weight ratios;  
C. Aldous, 11/19/86; Part of 057 937677.

167 048779 Individual body weights, body weight change, food      consumption and test  
substance intake data; C. Aldous, 11/19/86; Part of 057 937677.

168 048780 Individual maternal body weight data, gestation and lactation periods; C.  
Aldous, 11/19/86; Part of 057 937677.

077 937679 8/15/83 (Relates to 057 937677). Addendum: Pathology Report (Summary incidence of microscopic findings, terminal sacrifice); Contains pages 131-169 of full report); Part of J. Christopher, 7/10/85 review.

079 937678 7/6/80; J. Christopher, 7/10/85; Addendum to Pathology Report (Histopathology data on kidneys of low & mid-dose F3B males; includes historical background data for chronic nephritis); Part of 057 937677.

002 937676 Title: "Three-Generation Reproduction Study With CP 67573 in Albino Rats," IBT No. B566; IBT 7/26/73; J. Christopher 7/8/85 Glyphosate (no purity); Doses of 0, 30, 100, 300 ppm; Ruled valid but unacceptable by EPA.

022 025279 6/26/73 IBT Summary, Duplicate info. of 002 937676.

106 065474 Rebuttal containing the proposed protocol for: Two Generation Reproduction Study of Glyphosate in the Diet of Albino Rats. CDFA acknowledges the intent of Monsanto Company to repeat the rat reproduction study. M. Silva, 11/18/88.

\*\*364-206 095055 "Two generation reproduction feeding study with glyphosate in Sprague-Dawley rats". M.S. Reyna, Monsanto Agricultural Co., Environmental Health Laboratory, St. Louis, MO, 8/27/90. Study # 88038. Glyphosate, 97.67% purity, lot number XLI-203, fed in the diet continuously to two generations of Sprague-Dawley rats. F0 parents produced one litter and F1 parents produced two litters at 0, 2000, 10000, or 30000 ppm. There were 30 rats/sex/group. Parental NOEL = 10000 ppm (soft stools and reduced body weights at the high dose). Reproductive NOEL = 10000 ppm (reduced pup growth late in lactation). **No adverse effects. Acceptable.** (H. Green and C. Aldous, 7/31/92).

TERATOGENICITY, RAT

\*\* 121 035832 "Teratology Study in Rats", Study No. IR-79-016, IRDC, 3/21/80. Glyphosate, technical (98.7%); Doses of 0, 300, 1000 and 3500 mg/kg/day by gavage; Maternal NOEL = developmental toxicity NOEL = 1000 mg/kg/day. Developmental toxicity was seen only at dosages which cause substantial maternal toxicity. Reviews by J. Christopher 7/11/85 (judged unacceptable, with possible adverse effects); J. Parker 11/25/85 (judged the study unacceptable due to insufficient data, but not to indicate adverse effects, because developmental effects were observed only at the level which caused marked maternal toxicity. C. Aldous 11/20/86 (**Acceptable with additional data in 173 048856. No adverse effects.**)

173 048856 Rebuttal review by C. Aldous (11/20/86); Rebuttal (2 pages) plus Addendum (Individual antemortem observations, test article homogeneity & stability, protocol revision sheet, test article calculations, test material preparation records, Individual rat test material administration and observation records, Individual necropsy observations & summary); Part of 121 035832.

058 937672 IRDC Historical Control Data: Charles River COBS CD Rats (3 pages of tables); J. Christopher 7/11/85; Supplemental information to 121 035832. Reviewer considered increased resorptions, decreased fetal body weight, and increased numbers of unossified sternebrae as a "fetotoxic" response. (See updates in later reviews).

058 937674 Partial duplicate of 121 035832 (14 pages duplicate text plus 2 pages duplicate tables); see also comments by EPA staff and response by Monsanto at front of Part C.

022 025277 3/21/80 Summary, Duplicate information of 121 035832.

#### TERATOGENICITY, RABBIT

\*\* 121 035831 "Teratology Study in Rabbits", Study No. IR-79-018, IRDC, 2/29/80; Glyphosate technical (98.7%); Doses of 0, 75, 175 and 350 mg/kg gestation days 6-27 by gavage to Dutch Belted rabbits; Maternal toxicity NOEL = 175 mg/kg/day (high mortality, misc.

clinical signs at 350 mg/kg/day). Developmental toxicity NOEL = 175 mg/kg/day (highest dosage without excess maternal mortality). Reviews by J. Christopher 7/8/85 (insufficient information for assessment), J. Parker, 11/24/85 (unacceptable, needed additional data; no adverse effects, developmental NOEL = 350 mg/kg/day). Rebuttal (and additional data) review by C. Aldous, 11/21/86: **No adverse effects:** Developmental effects NOEL set at 175 mg/kg/day, the highest dose with sufficient surviving litters to assess developmental toxicity, however review noted that there was no developmental toxicity observed in the 6 litters delivered of 350 mg/kg/day dams). **Acceptable** on the basis of additional data.

058 937673 12/01/80; J. Christopher 7/8/85; IRDC Historical Control Data: Dutch Belted Rabbits (3 pages of tables); Supplemental to 121 035831.

172 048855 (9/30/86, Rebuttal/additional data to study, 121 035381); C. Aldous, 11/21/86: Rebuttal (2 pages); Attachment 1, (Individual maternal antemortem, necropsy & pathology observations, analytical methods, homogeneity & stability data, protocol revision sheet; Attachment 2, (Test article calculations, test material preparation records, individual rabbit test material administration and observation records).

058 937675 2/29/80 Partial duplicate of 121 035831 (16 pages duplicate text, 2 pages duplicate tables).

022 025278 2/29/80 Summary; Duplicate information of 121 035831.

002 937670 Title: "Teratogenic Study With CP 67573 In Albino Rabbits," 6/30/72 IBT; IBT Study No. J568; Dose levels of 10 or 30 mg/kg Days 6-18: Invalid.

#### MUTAGENICITY, GENE MUTATION

\*\* 057 937684 "Microbial Mutagenicity Testing on CP67573 (Glyphosate)," Institute of Environmental Toxicology; 7/20/78; S. typhimurium (TA 1535, TA 1537, TA 1538, TA 98, TA 100),

also E. coli WP2 hcr; Glyphosate (98.4%) at 0, 10, 50, 100, 1000 and 5000 ug/plate; 2 plates/group; No mutagenicity indicated; **Acceptable**. J. Christopher, 7/9/85 & 7/11/85.

057 025275, 025274 7/20/78 Summary, Duplicate info. of 002 937684.

\*\* 100 017462 "CHO/HGPRT Gene Mutation Assay with Glyphosate," Study No. ML-83-155, Monsanto, St. Louis, MO, 10/20/83; CHO cell line (K1BH4); Glyphosate (98.7%); Doses of 0, 2, 5, 10, 15, 20 and 25 mg/ml; No evidence of mutagenicity up to doses which cause greater than 50% cytotoxicity; **Acceptable**. J. Christopher, 7/18/85.

100 017463 "Glyphosate: Mutagenicity Studies, Over-all Assessment," no date (Justification of dose levels for 100 017462, 100 017461 and 100 017459).

057 033911 "Final Report on Salmonella Mutagenicity Assay of Glyphosate," Test No. LF-78-161, Monsanto, EHL, St. Louis, MO, 6/16/78; Ames spot test, plate incorporation & toxicity test; S. typhimurium (TA 100, TA 98, TA 1535, TA 1537); Glyphosate (98.4%); Spot test, 10 to 1000 ug/plate; Plate incorporation, 0, 0.1, 0.4, 1, 2, 10, 30, 100 and 1000 ug/plate; Toxicity test, 0.03, 0.1, 1, 3, and 10 ug/plate; Levels tested both with and without activation; Insufficient information for adverse effects assessment; **Unacceptable, Upgradable** (Needs toxicity test data, clarification of statistical methods used, description of microbiological methods. There is no apparent need to upgrade this study, as other studies are on file which fill this data requirement.) J. Christopher 7/11/85.

#### CHROMOSOMAL ABERRATIONS

058 937685 "Dominant Lethal Study in Mice," (IRDC, 4/16/80). Mouse dominant lethal (843). Glyphosate (98.7% purity) administered by oral gavage to 10 males/dose at 0, 200, 800, 2000 mg/kg, followed by sequential matings of 2 females/male/week for 8 weeks, a total of 160 females/dose. No mutagenicity observed upon sacrifice and examination of uteri. **Incomplete,**

**Unacceptable.** Too few animals, individual data missing. J. Christopher, 7/11/85 & B. Davis, 11/24/86.

169 048782 8/26/83; Response to CDFA review of 058 937685 on 7/11/85 (1 page, no data); B. Davis 11/24/86.

179 057543, Partial duplicate of 937685.

\*\* 100 017461 "In Vivo Bone Marrow Cytogenetics Study of Glyphosate in Sprague-Dawley Rats," DMEH Project. No. ML-83-236 (Monsanto 10/20/83). In vivo cytogenetics (843). Glyphosate (98.7% purity) administered i.p. to 18/sex/dose at 0 or 1.0 g/kg, sacrificed at 6, 12, or 24 hours, bone marrow cells scored for chromosome aberrations. No mutagenicity observed.

**Complete, Acceptable.** J. Christopher 7/18/85 & B. Davis 11/24/86.

100 017460 10/21/83 QA Statement; Bone marrow cell viability data (summary & individual), Appendices 1 & 2; J. Christopher 7/18/85; Part of 100 017461.

100 017458 8/26/86; "A Study of the Plasma and Bone Marrow Levels of Glyphosate Following Intraperitoneal Administration in the Rat," DMEH Project No. ML-83-218; Supplemental to 100 017461.

100 017463 "Glyphosate - Mutagenicity Studies, Over-all Assessment," no date (Justification of dose levels for 100 017462, 100 017461 and 100 017459).

169 048781 10/29/83 Response to CDFA review of 7/18/85 (100 017461), includes also Attachment 1 (EPA comments and Monsanto response). B. Davis, 11/24/86.

002 024951 Title: "Mutagenic Study With CP67573 in Albino mice" (Dominant Lethal), IBT No. E567; IBT, 1/24/72; J. Christopher 7/8/85; Dose levels 5 and 10 mg/kg: Ruled invalid by EPA.

022 025276 4/16/80 Summary, Duplicate information of 002 024951.

030 056909, 056910, Summary of 024951.

#### DNA DAMAGE

057 033913 "Microbial Mutagenicity Testing on CP67573 (Glyphosate)" (Institute of Environmental Toxicology 7/20/78). DNA damage (844). Glyphosate (98.4% purity) at doses of 0, 20, 100, or 200 ug/disk to B. subtilis matched strains H17 (repair-competent) and M45 (repair-deficient) in a disk diffusion, growth inhibition assay. No DNA mutagenicity observed. **Incomplete and Unacceptable.** Only single plates per treatment, doses tested from 20 to 200 ug/disk but reported as 20 to 2000. Reviews by J. Christopher, 7/9/85 and B. Davis, 11/24/86. Also examined by B. Davis as part of 12/7/87 rebuttal (no separate written review).

170 048783 8/26/86; Response to review of 057 033913 on 7/9/85; B. Davis, 11/24/86.

\*\* 100 017459 "The Hepatocyte Primary Culture/DNA Repair Assay on Compound JJN-1020 (Glyphosate) Using Rat Hepatocytes in Culture," Study No. AH-83-181; (Naylor Dana Institute for Disease Prevention 10/21/83). Glyphosate (98.7% purity) at doses from 1.25 X 10E-5 to 1.25 X 10E-1 mg/ml to primary rat hepatocyte cultures. UDS measured by autoradiography. **No adverse effect. Acceptable.** (Previously considered unacceptable by J. Christopher, 7/18/85, later by B. Davis, 11/24/86. Data in 179 057544 permitted status change to **acceptable** in B. Davis review of 12/7/87).

179 057544 "Data Submitted in Response to SB950 for Glyphosate In Vitro Hepatocyte UDS Assay." Raw data and supplementary information which made the study **acceptable with no adverse effect.** B. Davis, 12/7/87.

170 048784 8/26/86; Response to first review of 100 017459, discusses the adequacy of dose levels; B. Davis, 11/24/86.

100 017463 "Glyphosate - Mutagenicity Studies, Over-all Assessment," no date (Justification of dose levels for 100 017462, 100 017461 and 100 017459).



## NEUROTOXICITY

043/045 035918 Title: "Neurotoxicity Study with Chickens," IBT No. 8580-09117, IBT, 12/17/86. Initially reviewed by J. Christopher (7/8/85). Rebuttal review by C. Aldous (11/18/86). Invalid IBT study. **No adverse effect indicated and no replacement study required:** Test article is not in the class of compounds which require this test, and there are no indications from other tests suggesting that delayed neurotoxicity potential exists.

171 048785 Response to review on 7/8/85 of 043/045 035918.

022 025273 Summary; Duplicate information of 043/045 035918.

## MISCELLANEOUS IMPURITY STUDY SUMMARIES

The following summaries are either located under the title, "Summary of Toxicology Studies Conducted with N-nitroso Glyphosate (NNG)" in volume 364-045 or under the title, "Toxicology and Safety Assessment for N-Nitrosoglyphosate", pp. 12-16 in volume 364-071. N-nitroso Glyphosate is a manufacturing impurity of glyphosate found at very low levels. The following summaries have been reviewed by CDFA toxicologist, R. Wang, who concluded that "Roundup herbicide and its nitrosoglyphosate contaminant do not appear to pose unreasonable health hazards to users and consumers" (memo from the beginning pages of Volume 071). Of the studies which follow, most report clearly negative results. **CDFA requests a copy of the full report summarized as Record #35925 (IBT study BTL-76-32)**, which indicated an increase in resorptions and decrease in 24-hr survival of offspring in a rabbit teratogenicity/reproduction study. No worksheets have been generated by Medical Toxicology Branch on the following studies.

045/071 035923 "Mutagenicity Evaluation of CP76100;" Salmonella (5 strains) and Saccharomyces (strain D-4); Litton Bionetics; BIO-76-116; No report date; N-nitroso Glyphosate; No mutagenicity indicated; **Very brief summary.**

045/071 035924 "Dominant Lethal Study with CP76100 in Albino Mice," BTL-76-31; NNG at 5 or 10 mg/kg by i.p. injection; No lab or report date; **No adverse effect indicated; Very Brief Summary.**

045 035925 "Teratogenic Study with CP76100 in Albino Rabbits;" Lab and report date not stated; N-Nitrosoglyphosate (Glyphosate manufacturing impurity) at 0, 10 or 30 mg/kg days 6-18 of gestation by gavage; Increased resorptions, decreased numbers live young per 100 implantation sites and reduction in 24-hour survival at 30 mg/kg; **Very Brief Summary.**

071 No record #; 3-Generation Reproduction - Rat (834); BTL-76-34; Lab and report date not stated; NNG at 0, 3, 10 and 30 mg/kg by gavage; **No adverse effects indicated; Very Brief Summary.**

045/071 035926 "Eighteen Month Oral Toxicity Study in Hamster;" No lab or report date; Study actually run 12 months due to excessive non-treatment-related deaths in all groups; NNG at 0, 3, 10 or 30 mg/kg/day by gavage; **No adverse effect indicated; Very Brief Summary.**

071 No record #; Chronic - Rat (831); BTL-76-35; Lab & report date not stated; NNG at 0, 3, 10 OR 30 mg/kg for 2 years by gavage; **No adverse effects indicated; Very Brief Summary.**

071 No record #; Chronic - Dog (831); BTL-76-33; Lab & report date not stated; NNG at 0, 3, 10 or 30 mg/kg/day by gelatin capsules for two years; **No adverse effects indicated; Very Brief Summary.**

071 No record #; Onco - Mice (832); IRD-77-223; IRDC; Report date not stated, but this summary based on an interim report (in-life effects data only); NNG at 0, 50, 150 and 500 mg/kg/day for 24 months by gavage; **No adverse effects indicated; Very Brief Summary.**

#### MISCELLANEOUS IBT STUDY SUMMARIES

The following summaries are located under the title, "Summary of Available Toxicity Data with Glyphosate & Roundup Herbicide: Mutagenicity/Reproduction/Teratogenicity" in volume 364-045 (1 & 1/2 pages). All these studies are either invalid or do not meet EPA guidelines.

045 035937 IBT No. 633-07507 ; Gene Mutation (842) Salmonella (5 strains) plus 1 strain Saccharomyces; No adverse effect indicated: Invalid.

045 No record #; IBT No. 633-07801; Rec-assay (844); B. subtilis and E. coli; No adverse effect indicated: Invalid.

045 035939 IBT No. 623-7508; Host-mediated assay with S. typhimurium and albino rats and mice (842); no mutagenicity indicated: Valid study.

045 035901 IBT No A2144: A testicular effects study in rabbits. Not a standard reproduction study. **No adverse effects indicated.** No additional information necessary. C. Aldous, 11/16/87. No written review.